REMARKS/ARGUMENTS

Reconsideration of this application is requested. Claims 34-37, 39-50, 52-55 and 57-88 are in the case.

I. THE ANTICIPATION REJECTION

Claims 34-38 and 47-56 stand rejected under 35 U.S.C. §102(b) as allegedly anticipated by Grunenberg *et al.* (US 5,849,752) (Grunenberg). That rejection is respectfully traversed.

In response, and without conceding to the rejection, claims 34-37, 47-50 and 52-55 have been amended to refer to "crystalline" moxifloxacin hydrochloride form A having an X-ray diffraction spectrum as set forth in the claims. Support appears in the application as originally filed at, for example, page 3, line 14. Claims 38, 51 and 56 have been canceled without prejudice, and new claims 77-88 are drawn to the crystalline moxifloxacin hydrochloride form A in tablet form. Support for tablets appears in Example 6. No new matter is entered.

The Action alleges that moxifloxacin hydrochloride form A is anticipated by Grunenberg in view of the reference therein to anhydrous moxifloxacin hydrochloride and moxifloxacin hydrochloride monohydrate. In response, the claimed invention is directed to a particular moxifloxacin hydrochloride form A which is characterized by specific X-ray, ^{13}C-NMR and IR spectra. This data is completely different from those characterizing both the anhydrous and the monohydrate moxifloxacin hydrochloride disclosed by Grunenberg. In particular, these differences are evident when the following comparisons are made:

Comparison of Grunenberg's Figures 4A-4B and table 2 with Figure 1 and table (X-ray) of the present case;

Comparison of Grunenberg's table 1 with Figure 3 (IR) of the present case;

Comparison of Grunenberg's table 3 with Figure 2 (^{13}C-NMR) of the present case.

The above differences are discussed in the present application in paragraphs [0025], [0027] and [0028]. In this regard, it is noted that X-ray analysis is the most well known and the most widely used technique to identify polymorphs (see Otsuka, page 852 Material and methods; see also Jain, page 317 §iii).

The Action alleges that a formulation containing the instant compound (moxifioxacin hydrochloride form A) would be the same as Grunenberg's formulation containing anhydrous or monohydrate moxifloxacin hydrochloride. In support of such an argument, the Action relies on Chemical & Engineering News, pages 33-34. However, that document states that the efforts in API development should be focused on "understanding...how unit operations such as granulation, compaction, and tableting affect crystal structure".

Thus, it is well known in the art that crystalline forms **may** lose their unique crystalline structure when subjected to granulation, compaction, and tableting, but this does not necessarily mean that such changes **must** happen. Consequently, the Office has failed to provide unambiguous evidence that the presently claimed invention is disclosed by Grunenberg, literally or inherently.

In further support of this, attention is directed to the attached Rule 132 declaration executed by Stefano Turchetta (the Turchetta Declaration) which reports the

results of two compression tests performed on the presently claimed active principle, and solubility tests. Referring to the compression tests, in the first, the active compound was pressed in pure form into a tablet and, in the second, the active principal was mixed with the same excipients as described in Example 6 of the present application and then pressed into a tablet. The details of what was done and the results observed are presented in Exhibits 1 and 2 attached to the declaration. The obtained results clearly demonstrate that the new form A of the present invention retains its specific and characterizing crystalline form after compression. In the solubility tests, crystalline moxifloxacin hydrochloride form A of the present invention was compared with the monohydrate moxifloxacin hydrochloride disclosed in Grunenberg, and the results show that the crystalline moxifloxacin hydrochloride form A of the present invention is more soluble than the monohydrate moxifloxacin hydrochloride of Grunenberg.

As the claims now recite formulations and methods based on moxifloxacin hydrochloride form A having (and maintaining) a specific crystalline form, it is clear that Grunenberg does not anticipate the claimed invention. Withdrawal of the anticipation rejection is accordingly respectfully requested.

II. THE OBVIOUSNESS REJECTION

Claims 34-38 and 47-56 are rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Grunenberg in view of Chemical & Engineering News, Feb. 2003, Brittain *et al.* (Polymorphism in Pharmaceutical Solids, pages 1-2, 183-226), US Pharmacopia, *1995*, pp 1843-1844, Muzaffar *et al.* (J. of Pharmacy (Lahore) 1979, 1(1),

59-66), Jam *et al.* (Indian Drugs, 1986, 23 (6), Taday *et al.* (J of Pharm. Sci, 92 (4), April 2003, 83 1-838) and Concise Encyclopedia Chemistry, page 872-873 (1993).

In response, the attached Turchetta Declaration demonstrates that there is a difference in solubility between the instant claimed crystalline form A and the crystalline form described in Grunenberg. In particular, in the Turchetta Declaration, it is demonstrated that the instant claimed form A has a higher solubility compared to the monohydrate of Grunenberg. Therefore, the presently claimed crystalline form A solves the technical problem of having a more soluble (thus more readily bioavailable) crystalline form of the API.

Based on the above, it is clear that the cited art would not have suggested the claimed invention to one of ordinary skill in the art as of the filing date of the application. Withdrawal of the obviousness rejection is respectfully requested.

III. THE FORMAL REJECTION

Claims 47-56 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement as well as failing to comply with the enablement requirement. Based on the claim amendments presented herewith, it is believed that the specification provides an enabling disclosure of the claimed invention as well as an adequate written description of the invention as claimed. Withdrawal of the formal rejection is respectfully requested.

Favorable action is awaited.

Respectfully submitted,

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Attachment: Executed Rule 132 Declaration with Exhibits 1 and 2